The Lipids in Pathology of the Eye

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Abstract

The lipoidal composition of the human eye is frequently altered in the diseased state. Unfortunately, most of the literature is unreliable and only recently has adequate methodology been employed to determine the status of the lipids in ocular pathology. The modern studies have been very useful in helping to understand the mechanism behind some pathological problems and in a few cases, the lipoidal composition of a tissue has been elucidated and is presented herein for the first time.

Introduction

THE LIPIDS RANK AMONG THE EARLIEST analyses made on the eye. Aside from the importance of these compounds in healthy living tissue, their concentrations are frequently altered in the diseased eye where they appear as localized deposits resulting from lipoidal infiltration or degenerative processes. Unfortunately much of the literature on ocular lipids is based on poor analytical procedures. Moreover, erroneous animal data adds to the misunderstanding when it is transposed to explain human pathology. With new data obtained by modern analytical techniques it is possible to place the functional role of ocular lipids in a better perspective.

Sclera

The sclera comprises approximately 83% of the outer covering of the eyeball (Fig. 1). It is a tough, white, opaque tissue with a fibrous structure composed of collagen fibrils imbedded in a matrix of mucopolysaccharide. The scleral fibrils are arranged in bundles that form a random pattern of interdigitation which provides the tissue with its structural strength.

Scleral pathology usually does not involve the lipids. In the aged, however, lipoidal deposits may appear that give a yellowish coloration (1).

Scleral lipids of the beef eye only have been studied. Krekeler (2) was the first to demonstrate that lipids occur in this tissue and that they increase with age and in scleral degeneration. The only attempt to separate the scleral lipids was made by Krause in 1934 (3) who showed that although the sclera is not a lipid-rich tissue (0.62% of the fresh tissue), it nevertheless contains a complex mixture of lipids with glycerides and phospholipids predominating.

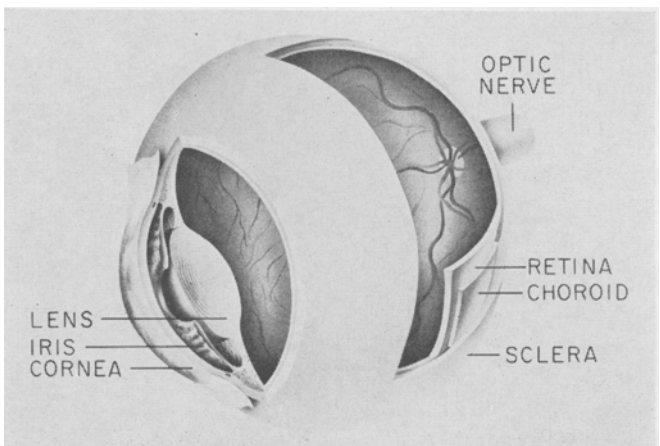

FIG. 1. Diagrammatic representation of the anatomy of the human eye showing the major structures to be considered in the text. (Courtesy Alcon Laboratories, Inc., Fort Worth, Texas).

FIG. 2. Microscopic section through the normal human cornea. The epithelial layer is multicellular, heavily stained and located at the top of this section. The bulk of the tissue consists of the fibrous stroma located between the epithelial layer and the one cell thickness of endothelium at the bottom of the section.

Cornea

The cornea is a transparent structure that covers the front of the eyeball and comprises the remaining 17% of the eye's outer covering (Fig. 1). It is a fibrous structure like the sclera, but its collagen bundles are organized into well-defined lamellae in the central portion. This stromal layer is the thickest portion of the cornea and is sandwiched between a multicellular layer of epithelium and a unicellular layer of endothelium (Fig. 2). The stroma and endothelium are separated from each other by an acellular structure known as Descemet's membrane. This layer is composed of an orderly lattice of fibers with a periodicity of 1000A (4,5) and may contain lipoproteins (6).

The most common disease of the cornea, arcus senilis, is characterized by the appearance of an infiltrate of cholesterol and cholesterol esters (7) which forms a ring around the corneal periphery (Fig. 3). The lipoidal material is usually concentrated in two wedge-shaped areas of the stroma adjacent to the epithelium and to Descemet's membrane and is readily demonstrated by staining with Sudan III (Fig. 4).

A similar lesion can be experimentally induced in the rabbit (8) by the feeding of cholesterol and

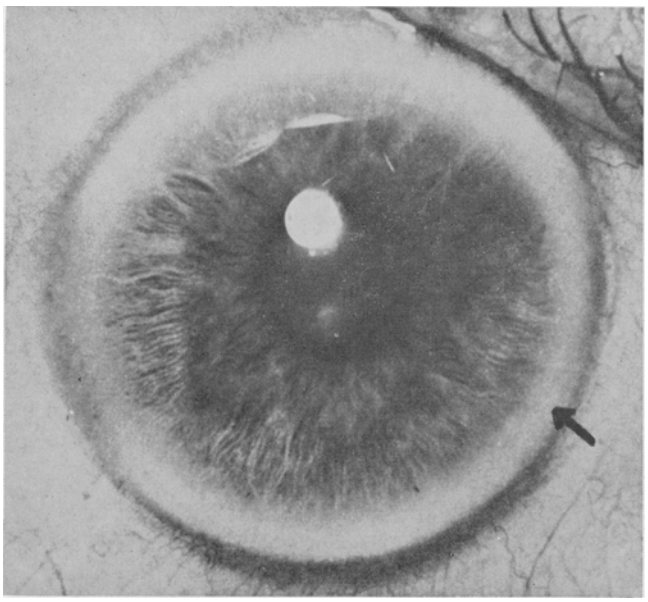

FIG. 3. Gross appearance of arcus senilis of the cornea. The arrow points to the ring of lipoidal material that characterizes this common disease.

probably occurs as a result of an infiltration of the lipid rather than a degenerative process (9). The simultaneous feeding of fat produces a greater degree of lipoidal infiltration (10). The experimental arcus of the rabbit unlike that of the human, reportedly contains only a small amount of cholesterol (11–16). However, this conclusion is suspect since it is based on nonquantitative histochemical evidence.

Another disease of the cornea is the so-called lipoidal dystrophy, characterized by the occurrence of a fatty plaque in the cornea. Cogan and Kuwabara (17) reported that such lesions occur predominantly in patients with hypercholesteremia when the normally avascular cornea has become vascularized. It can be experimentally induced in rabbits under similar conditions. Indeed, earlier workers had established that cholesterol esters can precipitate in large masses in the human cornea during hypercholesteremia (18–27), although this is not always a necessary consequence of this condition (28). It still remains to be determined whether there is a causal relationship between such lipoidal deposition in the cornea and serum lipid levels or whether some other factor such as the corneal vascularization mentioned by Cogan and Kuwabara is necessary for such a lesion to form.

The human corneal lipids were partially separated by Andrews (7) who demonstrated that the neutral lipids predominated and in arcus senilis were elevated in concentration. A similar conclusion was reached

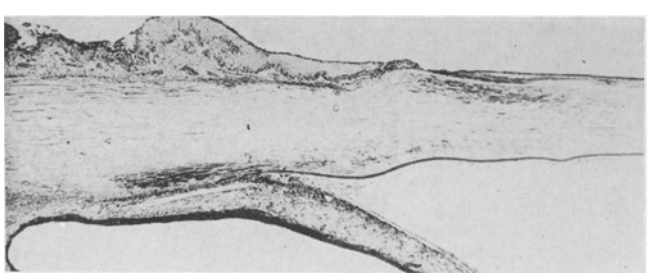

FIG. 4. Microscopic section through a human cornea with arcus senilis. The lipoidal deposits are seen as darkly stained areas. (Reproduced by permission from M. J. Hogan and L. E. Zimmerman, "Ophthalmic Pathology," 2nd Edition, W. B. Saunders Co., Philadelphia, Pa.).

TABLE I

Lipoidal Composition of Human Cornea[a]

Lipid class	% of Total
Neutral lipids	34.1
Gangliosides	16.1
Sphingomyelin	24.3
Phosphatidyl choline	2.2
Phosphatidyl ethanolamine	0.7
Phosphatidyl serine	5.0
Acidic lipids	13.0
Unidentified polar lipids	4.6
	100.0

[a] Based on pooled extracts of 15 normal human corneas removed at autopsy. Average dry weight of cornea is 21.76 mg. Reliable wet weights were not obtained. The average total lipid content per cornea was 1.08 mg.

by Tschetter (29), but his analytical data are questionable because of the extreme variation in triglyceride concentration (216–3517 γ/pair of corneas) that he obtained. The average neutral lipid concentration of human cornea obtained in our laboratory (30,31) is in excellent agreement with Andrew's data. The total lipid concentration that we obtained (Table I) is considerably higher because of the occurrence of the gangliosides which both Andrews and Tschetter failed to observe and because of a higher yield of other polar lipids.

The cornea is one of the few ocular tissues capable of synthesizing a lipid. Andrews and Kuwabara (32) reported that the rabbit cornea synthesizes triglycerides in vitro from either sodium oleate or glucose in the presence of serum. In a later study, Andrews (33) showed that the calf cornea synthesized both sterols and fatty acids from glucose and acetate. The demonstration of the presence of lipogenic enzymes in the cornea is of interest in view of the occasional suggestion that a defect in corneal lipid metabolism may cause the formation of corneal lipid deposits. Hopefully, additional studies will answer this question.

Aqueous Humor

The posterior face of the cornea is bathed in a fluid medium known as the aqueous humor. It is not a tissue and its lipid components are confined primarily to minute quantities of steroids (34) and lipoproteins (35). Normal aqueous humor contains no cholesterol (36) and only in rare cases of cholesterolosis bulbi (37) are cholesterol crystals seen to accumulate (Fig.

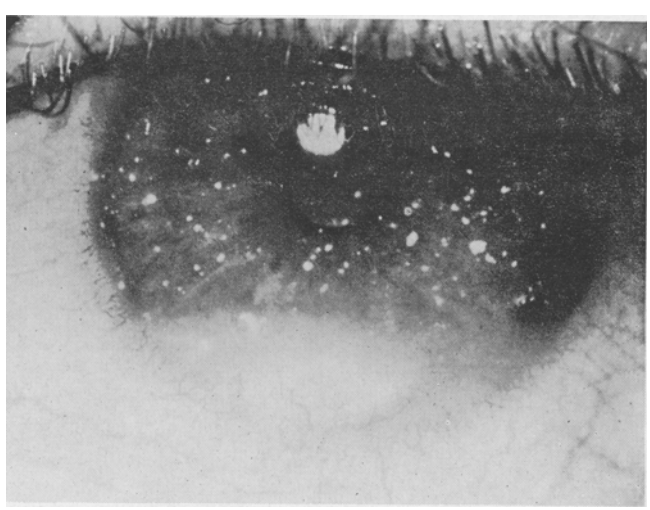

FIG. 5. Cholesterolosis bulbi of the anterior chamber. The dense white deposit in the lower quadrant of the eye is an accumulation of cholesterol crystals. The flecks above the deposit are crystals of cholesterol suspended in the aqueous humor (Courtesy Dr. Oliver Dabezies).

5). In the illustrated case (courtesy Dr. Oliver Dabezies) the aqueous humor was aspirated from the anterior chamber of the eye and the presence of cholesterol was determined by chemical analysis. The patient ultimately lost the eye. After its removal, it was found that cholesterol crystals had also accumulated in the subretinal fluid.

Attempts to treat such cases by aspiration of the crystals have not been successful. In one case (report of Dabezies) as many crystals were present on the day following aspiration as there were initially. It is noteworthy that most cases of cholesterolosis bulbi have a history of concussive injury to the eye accompanied by intraocular hemorrhage. This suggests that the cholesterol is a residue remaining after the dissolution of the hemorrhage. However, this mechanism does not explain the abundant recurrence of the crystals within 24 hr after aspiration.

Iris

The iris is a heavily pigmented tissue located between the cornea and the lens. By altering the diameter of its centrally located aperture (pupil) it controls the intensity of light passing into the eye. Except for histological evidence for the occurrence of Sudanophilic material in the iris in cases of arcus senilis, there is no discrete pathology in which lipids accumulate in the tissue. Very little is known of the lipid composition of this tissue. Aenggard and Samuelsson reported (38) the occurrence of a prostaglandin in the iris which may be the "irin" that Ambache (39) has shown to function in pupillary constriction.

Lens

The lens is an ellipsoid structure that has no vascular or nervous system. It is located behind the iris (Fig. 1) and held in place by tiny collagenous fibrils known as zonules that press it against the face of the vitreous body.

The cellular architecture of the lens consists simply of a monocellular layer of epithelial cells that cover only the anterior face and of lens fibers. These fibers lie beneath the epithelial layer and are orientated in an antero-posterior direction. The whole structure is contained within an acellular, collagenous capsule.

The lens fibers that constitute the core of the tissue are differentiated from superficial ectoderm during the development of the fetus. Subsequent to birth, these cells undergo further changes that result in a loss of both their nuclei and mitochondria. This central portion of the lens is designated as the nucleus. It is surrounded by other fibers that constitute the lens cortex. Unlike the cells of the nucleus, cortical cells contain subcellular particles.

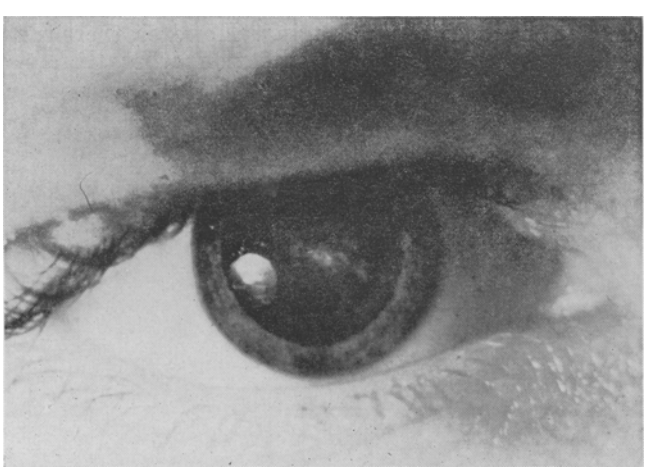

FIG. 6. Gross appearance of a typical cataract shown here as a dense white area in the center of the pupil. The large white area at one side is a light reflection.

TABLE II
Sterol Content of the Lens[a]

Specie	No. Analyzed	Wet Wt, g	mg sterol/g wet wt. Cholesterol	mg sterol/g wet wt. Desmosterol
Normal human	25	0.190	4.18	0
Triparanol-treated human	9	0.187	4.15	0
Senile cataracts	200	0.196	4.93	0
Rat (age 4 wk)	20	0.021	0.45	0.04
Rat (age 9 wk)	10	0.032	0.46	trace
Rat (age 9 wk, fed 0.1% triparanol for 4 wk)	10	0.031	0.44	0.02
Rat (age 20 wk)	10	0.049	0.52	0
Rat (age 20 wk, fed 0.15% triparanol for 81 days	4	0.047	0.46	0
Rat (age 2 yr)	6	0.059	0.63	0
Rabbit (age 4.5–5.5 kg)	150	0.540	0.71	0
Bovine (age 1 yr)	80	1.390	0.65	0

[a] Work done in collaboration with J. F. R. Kuck, Jr., Dept. of Ophthalmology, Emory University, School of Medicine, Atlanta, Georgia.

The lipids are intimately involved in cataract, the only disease of the lens. Cataract is characterized by an opacification (Fig. 6) which frequently results from the death of the lens fibers. Since there is no vascular system in the lens, there is no phagocytosis. Consequently, cellular debris remains in place, trapped there by the live cells around it.

For many years it was believed that cataract was an accumulation of cholesterol (40). The human lens is normally rich in cholesterol (Table II), a fact known to the ophthalmologists since the early 1800's. Most of the early studies showed a marked increase in cholesterol concentration in cataracts, but by the 1960's there were sufficient reports to the contrary so that the relationship of cholesterol to the disease was questionable.

In 1965, Feldman and Feldman (41) reported the occurrence of a lipid-protein complex in human lens and demonstrated that a breakdown of the complex occurs in cataracts. The disease does not alter the total lipid content of the lens but only affects the distribution of the lenticular lipids between protein bound and unbound forms. When the amount of protein bound lipid is reduced, there is a concomitant increase in the amount of unbound lipid (Table III). It therefore seems highly probable that the increase in cholesterol content of cataractous lenses reported by earlier investigators was actually an analysis of the increase in unbound sterol as a result of the breakdown of the complex rather than an analysis of total sterol which is unchanged.

The decrease in the amount of protein-bound lipid is similar to an observation reported by Efet (42)

TABLE III
Distribution of Lipids in Normal and Cataractous Human Lenses[a]

Form of occurrence	% of Total lipid Normal	% of Total lipid Cataract
Unbound form		
Neutral lipids	25.0	35.5
Polar lipids	8.4	22.1
Proteolipid form		
Neutral lipids	25.8	14.9
Polar lipids	40.8	27.5
	100.0	100.0

[a] Based on pooled extracts from 120 cataractous lenses and 25 normal lenses. Average lipid content of the two groups is 4.76 mg/normal lens and 4.62 mg/cataractous lens. The average age of the normal group was 62 years whereas the cataractous group was 60 years. The slightly higher lipid content of the normal group is probably due to this age differential.

that the lens contains "lipoproteins" and that in cataracts the cholesterol content of an insoluble fraction (that might be proteolipid which is insoluble in water, but soluble in organic solvents) decreases with a corresponding increase in the cholesterol content of a water-soluble lens protein. Efet also found a 1.5 fold increase in total lenticular sterols in senile cataracts (42). We have found no such difference between senile cataracts and normal lenses of the same age. This lack of agreement may be due to the fact that Efet's control group was much younger than his cataractous group. Since the human lens normally increases in cholesterol concentration by approximately 10 μ g per year (43), the difference that he observed could be due to age and not the disease. Some of Efet's later studies with human cataracts from electrical shock (44) and experimentally-induced cataracts in rabbits (45) indicated the same change in distribution of cholesterol between the two lenticular proteins, but unlike senile cataracts, there was no increase in total cholesterol. The control groups were of the same age as the cataractous group in these two studies. Thus, the failure to observe an increase in total cholesterol in these cases could reflect their similarity in age rather than a difference in etiology of the disease as Efet suggested.

Cholesterol crystals (Fig. 7) are occasionally seen in the lens (46). This condition differs from the more common cholesterolosis bulbi in that it occurs without a previous history of concussive injury.

Attention was once again drawn to lenticular cholesterol following reports of cataract in patients treated with triparanol (MER-29) to control hypercholesteremia (47–50). The drug inhibits the conversion of desmosterol to cholesterol (51). The decrease in serum cholesterol is usually accompanied by an increase in desmosterol (52), which led Minton and Bounds (50) and von Sallmann et al. (53) to suggest that desmosterol may increase in the triparanol-induced lesion. We found no such increase in a group of cataractous lenses from patients treated with MER-29 (Table II). However, since the lesion appeared in most cases after withdrawal from the drug, it is possible that the desmosterol was depleted before the tissue was analyzed.

It is noteworthy that the lenses of immature rats contain desmosterol (Table II) that disappears as the animal ages. Triparanol delays this depletion, but has only a small effect on the lenticular cholesterol concentration even after 81 days of feeding (Table II). The blood serum, adrenals and livers of the triparanol-fed animals all contain large amounts of desmosterol which becomes evident as early as 48 hr after drug feeding is begun. It thus appears that the ingestion of triparanol does not produce an accumulation of lenticular desmosterol in the rat. Moreover, none of the animals developed cataracts.

Von Sallmann et al. (53) reported in an earlier study that a diet supplemented with 0.10% triparanol induced cataracts in rats in from 10 days to 16 weeks of feeding. However, this study did not involve chemical analyses of the tissues, was without a control group fed the unsupplemented diet and was further complicated by a high, unexplained death rate among the animals during the first weeks of the experiment. We failed to induce cataracts with 50% higher levels of triparanol feeding of rats for approximately the same length of time that these authors reported. Furthermore we found no such high early mortality in our studies. Thus the conclusion is questionable that the drug is cataractogenic to the rat when administered as a dietary supplement. Moreover, triparanol feeding did not lead to an accumulation of desmosterol in the lens as it did in other tissues. Thus von Sallmann's report of cataract induction in rats fed triparanol may have been related to the unexplained illness in the rat colony. The cataractogenic nature of this drug in the human is equally questionable.

The lipids of the human lens, in addition to an abundance of cholesterol, contains large amounts of sphingomyelin, gangliosides and neutral glycolipids (41,54–57). The composition of the mixture is shown in Table IV. It is particularly interesting to compare the similarity of this analysis with that of the cornea (Table I). Most of the lipids occur in the membranes of the lens fibers (58). The sphingolipids are saturated and chemically stable compounds, whose occurrence in these membranes probably lends them structural strength.

Triglycerides are a minor component of lenticular lipids constituting approximately 174 γ in an adult human lens. Unlike cholesterol, which increases with age, the lenticular triglycerides are diminished in concentration in older age groups (59). In the gas chromatographic analysis of these compounds, a group of peaks elute that could be short chain triglycerides (60). It is possible that the lens slowly degrades its triglycerides and that this results in the lowered concentration associated with aging. However, there is no evidence to support this contention other than the diminution of concentration.

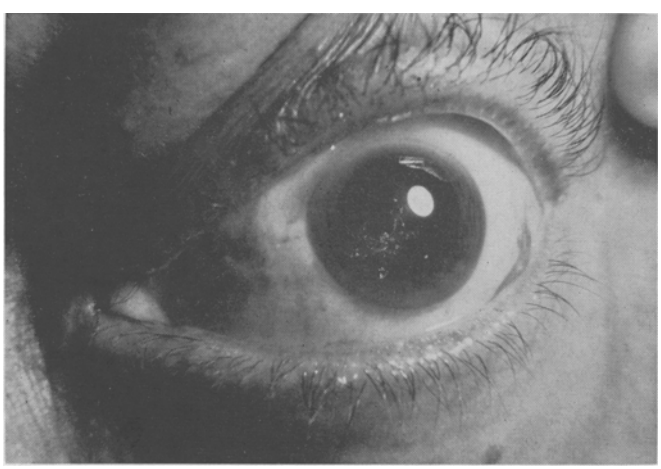

FIG. 7. Gross appearance of cholesterol crystals in the lens. The patient, a 74-year-old Negro woman, had a cataract in the other eye and is diabetic. The crystalline deposit does not adversely affect her vision nor does it interfere with her occupation as a seamstress. Analysis of the blood serum showed the cholesterol concentration to be within normal limits.

TABLE IV

Lipoidal Composition of Normal Human Lens[a]

Lipid class	% of Total
Neutral lipids	50.9
Gangliosides	5.4
Sphingomyelin	26.8
Phosphatidyl choline	1.1
Phosphatidyl ethanolamine	3.5
Phosphatidyl serine	1.3
Phosphatidyl inositol	4.8
Phosphatidic acid	2.0
Unidentified polar lipids[b]	4.2
	100.0

[a] Based on pooled extract of 25 normal human lenses. Average wet weight of 190 mg, average dry weight of 65 mg, average total lipid content is 4.76 mg.

[b] Primarily composed of ceramide dihexoside that has not been quantitatively isolated (56).

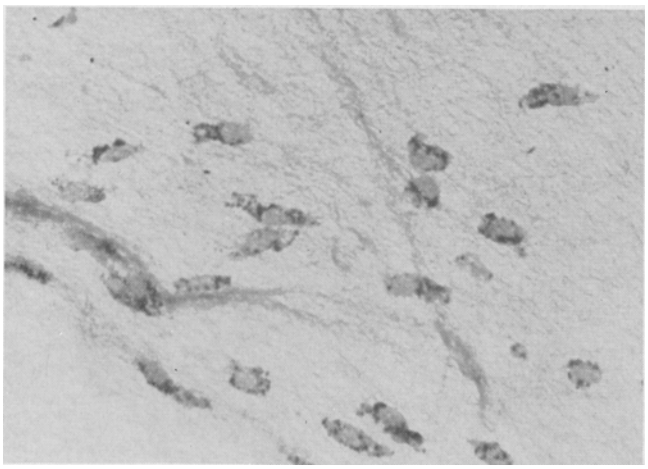

FIG. 8. Cells of the cortical vitreous. The heavily staining granules of these remarkable cells are rich in lipids. The cells are extremely difficult to isolate and photographs such as this are very rare.

Vitreous Body

Approximately two thirds of the eyeball's volume is filled with the transparent, gelatinous vitreous body which lies directly behind the lens and iris. Its structure is not completely defined although the existing evidence shows it to consist of a matrix of collagen fibrils embedded in a gel of hyaluronic acid (61). Vitreal cells primarily occur in the area in front of the retina. These cells are highly mobile, amoeboid in nature and contain large masses of cytoplasmic granules, some of which contain lipids (Fig. 8). The function of the vitreal cells is unknown. However, they are capable of synthesizing hyaluronic acid and may function as the source of this material for the vitreous body. Only 1% of the vitreous body is composed of dry matter, mostly hyaluronic acid and protein. For this reason, the occurrence of visible lipoidal deposits or any opaque particulate matter in vitreal pathology is a rather striking feature. One of the most dramatic of such pathological conditions is asteroid hyalitis (Fig. 9). In this disease the vitreous body contains numerous small particles whose gross appearance can be likened to stars in the sky and have the descriptive term "asteroid" hyalitis.

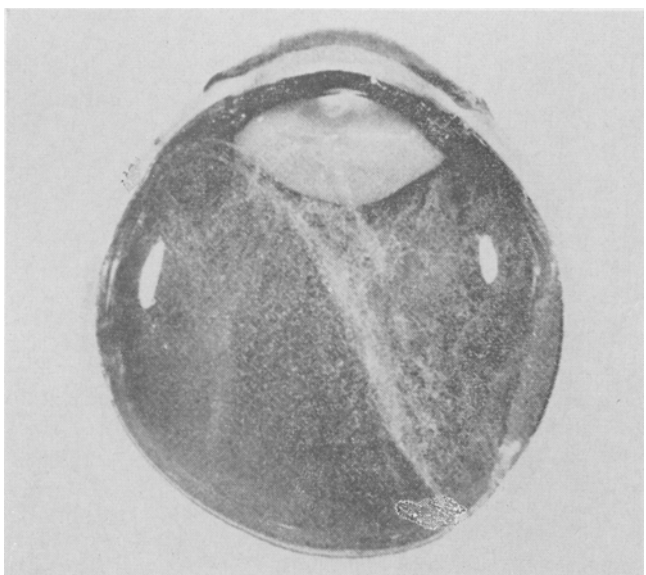

FIG. 9. Gross appearance of a typical case of asteroid hyalitis. The white particles scattered throughout the vitreous body remind one of the stars in the Milky Way and hence the name "asteroid" hyalitis (Reproduced by permission from M. J. Hogan and L. E. Zimmerman, "Ophthalmic Pathology," 2nd Edition, W. B. Saunders Co., Philadelphia, Pa.).

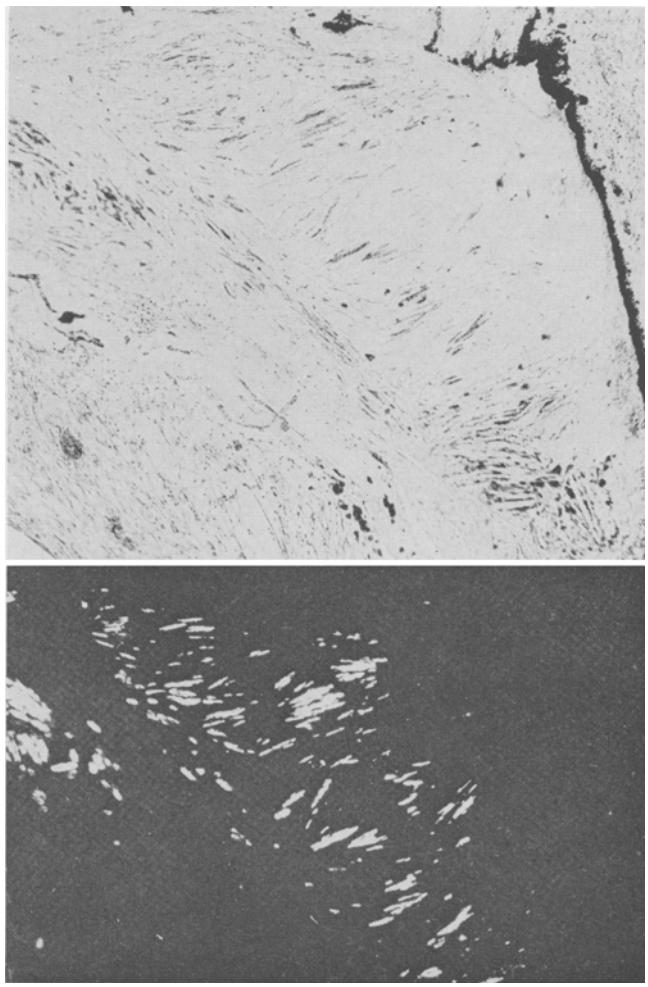

FIG. 10. Cholesterolosis bulbi of the vitreous body. This pathological condition is characterized by localized deposits of cholesterol that are readily observed under polarized light as shown in the lower figure. The transparency of the vitreous body makes visualization difficult under ordinary light as seen in the upper figure. There is some question of whether the deposit is cholesterol, cholesteryl esters or both (Reproduced by permission from M. J. Hogan and L. E. Zimmerman, "Ophthalmic Pathology," 2nd Edition, W. B. Saunders Co., Philadelphia, Pa.).

Although asteroid bodies are readily stained by the lipid stains, they are insoluble in most organic solvents. Verhoeff (62) suggested in 1921 that these particles may be composed of calcium salts of fatty acids. However, studies from our own laboratory (63) have shown that the asteroids do not contain calcium salts of fatty acids, but instead are composed primarily of sphingomyelin, ceramide dihexoside, traces of cerebroside, cholesterol and cholesterol esters. The apparent insolubility of the intact asteroid bodies is probably due to a protein component.

Cholesterolosis bulbi also occurs in the vitreous body (Fig. 10). This condition is characterized by localized deposits of cholesterol that are seen as birefringent crystals when examined under polarized light. The occurrence of cholesterolosis bulbi frequently follows other ocular disease such as trauma, hemorrhage or inflammation.

There is very little lipoidal material in the vitreous body and it is probable that what does occur is derived from the vitreal cells. Lohmeyer (64) in 1854 was the first to report the occurrence of vitreal lipids. In 1909,

Valentin (65) reported that the equine vitreous contained free cholesterol, cholesteryl esters, glycerides, choline phosphatides and fatty acid salts. Later studies of the bovine vitreous body by Jess (66) were essentially in agreement with Valentin's work, except for the observation that cholesteryl esters do not occur in the bovine vitreous body. These qualitative findings were confirmed by other investigators (36,67,68), but there is a lack of agreement on the concentration of vitreal lipids except that it is very low.

Much of the work on vitreal lipids has been concerned with the lipoidal deposits that occur in vitreal pathology (69–72). The relationship of these deposits to other ocular diseases was recognized as early as 1918 (69). Subsequent studies confirm this observation, but add little to our knowledge of either the chemical composition of the vitreal deposits or the mechanism for their formation. Regrettably, this area of investigation has not been pursued by contemporary investigators.

Retina

Most of the inner surface of the eye is covered with the highly organized cellular structure of the retina that extends rearward from a point posterior to the base of the iris (Fig. 1). We recognize the occurrence of two discrete and morphologically different portions of the retina. The inner portion is composed largely of rods and cones and constitutes the sensory retina. It in turn is composed of nine different layers that are all interconnected by broad contact between neural components and by a system of special supporting fibers (Fig. 11). The outer portion of the retina constitutes the pigment epithelium.

The preponderance of neural elements in the retina makes it very much like brain. This similarity is also seen in the large amount of lipid contained in the retina. Most of the work with retinal lipids has been concerned with the sensory layers and in particular with their Vitamin A content which is related to the visual process. This subject has been the basis for numerous reviews and is thoroughly documented in most modern textbooks of physiology. The most recent review may be found in "Biochemistry of the Retina," edited by Clive N. Graymore, Academic Press, New York, 1965. See also reference 93, pp. 196–204.

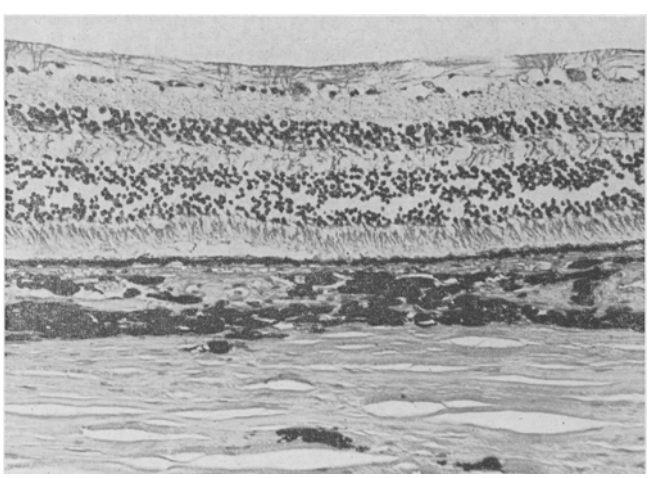

FIG. 11. Microscopic section through the normal human retina. The upper part of the section is the area adjacent to the inside of the eyeball. Light rays penetrate through the retina to its pigment epithelium. It is a fibrous area located directly above the heavy black deposits in the middle of the photograph. The deposits occur in the choroid and are pigment, characterizing this specimen as having come from a Negro.

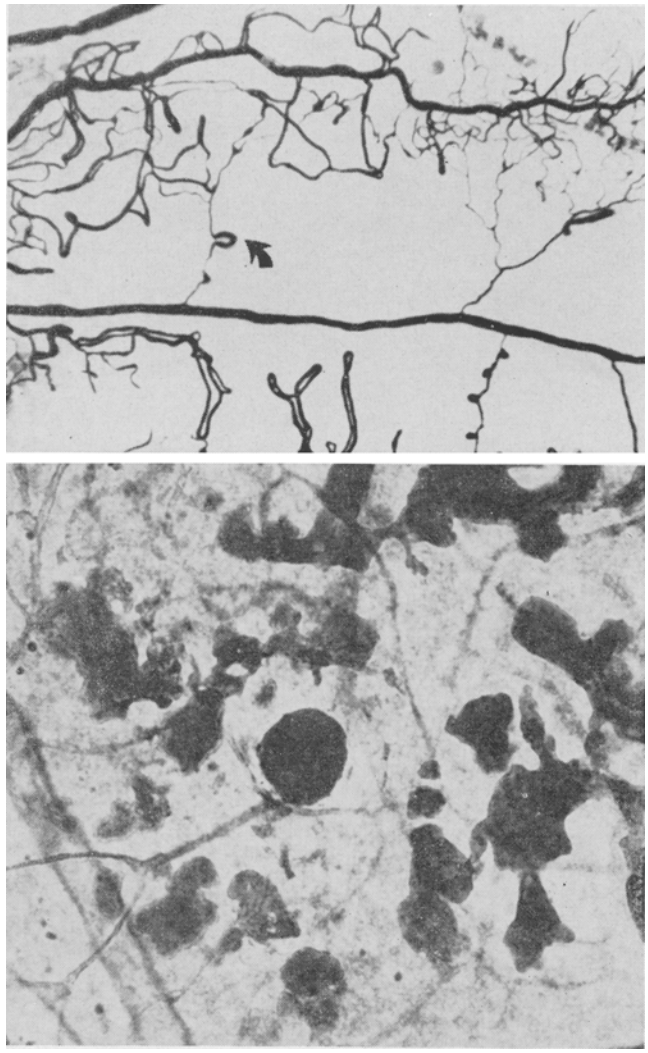

FIG. 12. A typical case of diabetic retinopathy. The photograph above illustrates the early stages of the disease in which micro aneurysms occur in the retinal blood vessels (arrow). These become occluded and surrounded by large amounts of lipoidal material that exude from the closed-off blood vessel as shown in the lower photograph at higher magnification.

It is not surprising that such a lipid-rich tissue will frequently demonstrate localized accumulations of lipoidal material that has been liberated from dead cells. In retinal degeneration associated with diabetes for example, the work of Ashton (73) has shown that the retinal blood vessels develop microaneurysms (Fig. 12) which at full development are surrounded by a lipid-rich exudate composed of mucoprotein and glycolipids (74,75).

The classical sphingolipidoses such as Tay-Sachs disease and Niemann-Pick disease are characterized by retinal changes. These usually parallel the brain changes associated with the diseases. A detailed description of the lipoidal degeneration that occurs in the retina in the sphingolipidoses may be found elsewhere (1).

Particles that are similar in appearance to asteroid bodies are sometimes seen in the area between the sensory retina and pigment epithelium (Fig. 13). These particles are often referred to as subretinal asteroids. Unlike the asteroids, these particles are readily soluble in alcohol and chloroform.

The lipids from two cases of subretinal particles were analyzed in our laboratory by thin-layer chroma-

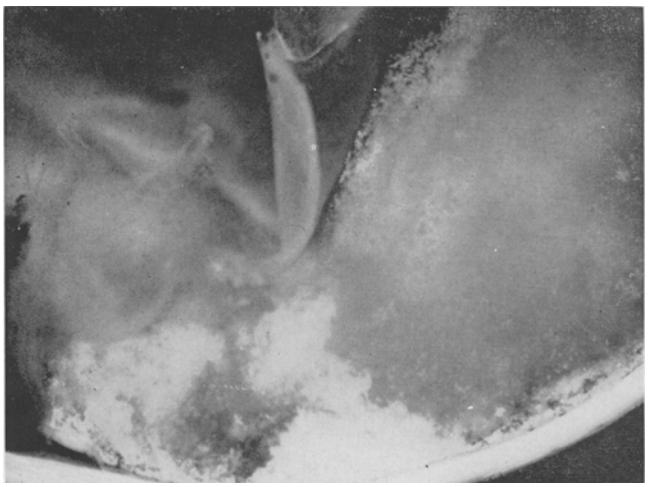

FIG. 13. Gross appearance of a case of subretinal particles. The cut edge of the sclera can be seen as a white, curved band at the bottom of the photograph. The retina has detached and lies in a fold at the top center of the photograph. The particles are copiously located in the subretinal space and appear as fluffy masses of crystalline material readily soluble in chloroform.

tography (TLC) and compared with the lipids of asteroid hyalitis (63). The subretinal particles appear to originate from small pieces of pigment epithelium. This can be seen by the formation of localized depigmented outcroppings (called drusen) on the inner face of the pigment epithelium (Fig. 14) which then are released to become the subretinal particles. A TLC analysis of lipids from the pigment epithelium established that it was predominantly cholesteryl esters, a previously unreported fact. Thus, the implication that subretinal particles arise from the pigment epithelium is at least a reasonable hypothesis since the two are chemically similar. Additional study is needed to verify this contention.

The retinal lipids have been the subject of investigation since 1879 when Kuhne (76) isolated lecithin from frog retina. Two years later Cahn reported the occurrence of lecithin in the retinas of cattle, pigs and horses (77). Subsequent investigators confirmed the lipid rich nature of the tissue and in particular, the abundance of choline containing phosphatides (78–91).

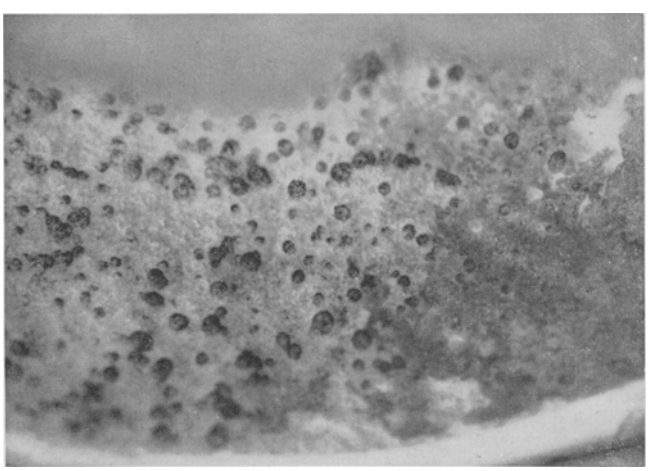

FIG. 14. Gross appearance of drusen on the retinal pigment epithelium. The cut edge of the sclera can be seen at the bottom of the photograph which is orientated for comparison with the previous figure. It is believed that the subretinal particles are derived from these drusen which become depigmented and then break loose from the pigment epithelium to become the particulate masses seen in the previous photograph. The particles, drusen and pigment epithelium are very rich in cholesteryl esters, suggesting a relationship in origin.

For many years it was believed that the retina contained only lecithin and cholesterol. However, in 1944, Böck (81) demonstrated a strong Schiff's positive reaction in human ocular tissue including retina. He interpreted this to indicate the presence of plasmalogens, but in view of reports of the occurrence of glycolipids in the retina (86,88–90), it seems more likely that the aldehyde groups of the carbohydrate moieties of these compounds were responsible for the phenomenon that he observed.

Much of the retinal lipid (in addition to Vitamin A) occurs as rhodopsin, which Krinsky (92) suggests is a lipoprotein. He points out that there are approximately 20 phospholipid residues per mole of rhodopsin. Rhodopsin has a molecular weight of 36,000–41,000 (93). This, together with its high lipoidal content and solubility in organic solvents, suggests however that it is a proteolipid rather than a lipoprotein.

The outer segments of the rods are particularly rich in lipids (94). When expressed on the basis of mg lipid phosphorous per 100 g wet weight of tissue, this portion of the retina contains over three times as much phospholipid (320.0) as the whole retina (92.5). Although these data may be inaccurate, they strongly suggest that the rod outer segments rank among the richest in lipids of the body tissues.

Reliable quantitative values for the retinal lipid composition are lacking. The existing literature is based on a variety of species and an array of strictly qualitative analytical procedures. Data on the human tissue is almost nonexistent. This is true not only for retina, but for all ocular tissues. This review points out deficiences that exist in our knowledge of ocular tissue lipids. Hopefully, it provides the basis for new research made promising by utilizing the superb analytical procedures now available.

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